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09/257,272	02/25/1999	JING-SHAN HU	PF112P2D2	1980

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EXAMINER

LANDSMAN, ROBERT S

ART UNIT	PAPER NUMBER
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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 09/257,272
Filing Date: February 25, 1999
Appellant(s): HU ET AL.

Melissa Pytel
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed May 6, 2004.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

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(2) *Related Appeals and Interferences*

The brief does not contain a statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief. Therefore, it is presumed that there are none. The Board, however, may exercise its discretion to require an explicit statement as to the existence of any related appeals and interferences.

(3) *Status of Claims*

The statement of the status of the claims contained in the brief is correct.

(4) *Status of Amendments After Final*

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) *Summary of Invention*

The summary of invention contained in the brief is correct.

(6) *Issues*

The appellant's statement of the issues in the brief is correct.

(7) *Grouping of Claims*

The rejection of claims 33-48, 65-96 and 113-272 (regarding obvious-type double patenting) and the rejection of claims 33-48, 65-96 and 113-160 (regarding written description) stand or fall together because appellant's brief does not include a statement that this grouping of claims does not stand or fall together and reasons in support thereof. See 37 CFR 1.192(c)(7).

(8) *Claims Appealed*

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) *Prior Art of Record*

No prior art is relied upon by the examiner in the rejection of the claims under appeal.

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(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Non-Statutory Double Patenting

A. Claims 33, 34, 49, 50, 65, 66, 81, 82, 97, 98, 113, 114, 129, 130, 145, 146, 161, 162, 177, 178, 193, 194, 209, 210, 225, 226, 241, 242, 257 and 258 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting over the claimed invention in the following copending U.S. Applications: 09/219,442, 09/935,726, 08/465,968 (U.S. Patent 6,608,182) and 09/107,997. Paper 32, Paragraph 3B. As stated in Appellants' previous response, on receipt of a Notice of Allowance, Appellants will either file a terminal disclaimer or cancel any conflicting claims that remain pending. As for the claims pending in Serial No. 09/935,726 and 09/107,997, Appellants acknowledge that a clear line of demarcation will be maintained as set forth in M.P.E.P. 822.

B. Claims 33-48, 65-96, and 113-272 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being obvious over claims 14, 15, 18-20 of copending U.S. Application 10/060,523, and claims 69-86 of copending U.S. Application 10/127,551. Claims 33, 34, 49, 50, 65, 66, 81, 82, 97, 98, 113, 114, 129, 130, 145, 146, 161, 162, 177, 178, 193, 194, 209, 210, 225, 226, 241, 242, 257 and 258 also remain provisionally rejected over one or more claims of U.S. Application 10/084,448. Appellants acknowledge these provisional rejections. Upon receipt of a notice of allowance, Appellants will file an appropriate disclaimer, to the extent that such a disclaimer is necessary, or will cancel any conflicting claims that remain pending.

C. The rejection of claims 38-48, 70-80, 86-96, 118-128, 134-144, 150-160, 166-176, 182-192, 198-208, 214-224, 230-240, 246-256, and 262-272 under the judicially created doctrine of obviousness-type double patenting as being obvious over claims 38 and 42-71 of U.S. Application 09/499,468 has been

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withdrawn in view of Appellants' cancellation of claim 38 and amendment to claim 42 to recite "a method of treating a patient having an injury to or degeneration of a photoreceptor cell" and to recite "a therapeutically effective amount" of the VEGF-2 protein. Neither of these claim amendments are disclosed or suggested by the claims recited in the above captioned application. Moreover, the process steps are not inherently taught by the above captioned application, since the treated patient must have "an injury to or degeneration of a photoreceptor cell." Therefore, the amendments to claim 42 in U.S. Application 09/499,468 obviates the provisional double patenting rejection.

Claim Rejections - 35 USC § 112, first paragraph – written description

Claims 33-48, 65-96 and 113-160 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims recite "mature" and "proprotein" forms of VEGF. However, the instant specification fails to describe that portion of a protein which is the "mature" portion, or what constitutes a "proprotein." Applicant is claiming a very specific species which is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The structure of a "mature form of a polypeptide" cannot be predicted on the basis of the amino acid sequence of the entire protein since the protein may be proteolytically cleaved in vivo, as well as being differentially processed based on in which tissue the protein is expressed. The claims are directed to a species of protein, the structure of which cannot be determined or predicted from full-length amino acid sequence and the specification does not evidence isolation or conception of the structure of the "mature form of a polypeptide," or the "preprotein form." Therefore, the specification does not provide an adequate written description of a mature protein,

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or preprotein form and thus the claimed invention, to the extent that it reads upon mature protein or proprotein was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

(11) *Response to Argument*

Non-Statutory Double Patenting

Appellants argue that, as a preliminary matter, this rejection is the sole remaining rejection of claims 161-272. With respect to the double patenting rejection, Appellants agree to file a Terminal Disclaimer in the present application over the currently pending claims that are or will be allowed/issued prior to allowance of the instant application. In this respect, Appellants note that Application Serial No. 08/465,968 issued as United States Patent No. 6,608,182 on August 19, 2003. Upon notification of allowable subject matter, Appellants will file a Terminal Disclaimer over at least United States Patent No. 6,608,182.

Claim Rejections - 35 USC § 112, first paragraph – written description

In the Response filed 10/15/03, as well as in the Appeal Brief, Appellants argue that a crucial step in determining the meaning of a technical claim term is to determine the ordinary meaning that would be ascribed by a person skilled in the relevant art. Additionally, technical publications can be used to confirm the skilled artisan's definition of a technical claim term, as well as to show that the patentee intended to apply that definition. Appellants argue that page 11, lines 11-21 of the specification defines the terms "mature" and "proprotein" and that these terms are consistent with those used in the art. They further argue that determining the amino acid sequence would be routine and that Appellants have provided a third party publication that demonstrates VEGF-2 is processed similarly in different cell types. Finally,

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Appellants argue that if one of skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if every nuance of the claim is not explicitly described in the specification, then the adequate written description requirement is met. Moreover, Appellants argue that at the time of filing it was well known how to N-terminally sequence isolated proteins from cells transfected with a particular gene sequence. Therefore, if necessary, the skilled artisan could have routinely expressed the VEGF-2 sequence disclosed in the specification and N-terminally sequence the isolated protein, thereby identifying the amino acid sequence of the mature form.

These arguments have been considered, but are not deemed persuasive. First, though the term "mature" and "proprotein" may very well have accepted meanings to those of ordinary skill in the art, the issue remains that Appellants have not provided adequate written description of the amino acid sequence of these forms. In other words, Appellants have not provided the specific sequences of the 'mature' and 'proprotein' forms of VEGF. Therefore, the skilled artisan would not know when they were in possession of the mature form or proprotein form of the VEGF receptor. These forms may, in fact, be identifiable by methods well-known in the art, or may be naturally and inherently expressed by a host cell (as argued by Appellants on pages 15 and 16 of the Appeal Brief), or is similarly expressed in various cells. However, the issue remains that Appellants have not provided the amino acid sequences of either of these protein forms. This written description (i.e. the exact protein sequence) may not be required for peer-reviewed journal articles. However, Appellants must be in possession of what is claimed. Therefore, the Applicant has not clearly allowed the artisan to recognize that the Applicant has invented what is claimed. Appellants' definition of these terms in the specification do not remedy this situation since, again, no detail as to the structure of the mature or proprotein forms has been provided. Perhaps the most persuasive argument the Examiner can provide is Figure 10 of Joukov et al. (page 3907) where the complexity of the pathway to produce the mature VEGF-C from the preproprotein (the one identical to the present invention) can be seen. The final product is a disulfine-linked homodimer in which one VEGF

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is in the reverse order of the other. Neither this pathway, nor the structure of the mature form have been described in the present application.

On page 10 of the Appeal Brief, Appellants argue that the Federal Circuit has held that the proper standard for written description is whether the artisan would have understood the inventor to be in possession of the claimed invention. In fact, whether the artisan would have understood the inventor to be in possession of the claimed invention is the exact issue in question. While terminology like "mature" and "proprotein" may be understood in the art as far as their literal meaning such as "a protein which has a structure such that..." (see pages 12, 13, 16 and 17 of the Appeal Brief) and that fact that cells would be able to produce "mature" proteins, the fact remains that the inventors did not know the exact amino acid sequences of the "mature" or "proprotein". Viewing the situation another way – the art-accepted definitions do not in any way provide information as to the specific structure of these forms of VEGF. Therefore, the artisan would not have known when the inventors were in possession of these proteins. To exemplify, if the artisan had dozens or hundreds of proteins in front of them, separated into groups based on sequence, and they needed to identify the "mature" protein, the artisan, given simply a dictionary definition of this term, or knowing that cells can inherently produce these proteins, would not have been provided with adequate written description to be able to identify which protein is the mature form. If, as Appellants argue, they were in possession of the mature or proprotein forms of VEGF, it should have been routine to have sequenced these forms. The fact that the full length VEGF protein of SEQ ID NO:2 was known and sequenced and that variants of SEQ ID NO:3 and 4 were also known and sequenced, as argued on page 12 of the Appeal Brief, still does not allow the artisan to identify the mature or proprotein form of SEQ ID NO:2 since neither SEQ ID NO:3 or 4 is the desired (claimed) sequence. Similarly, as argued on page 12 of the Brief, Appellants state that the specification (page 11, lines 15-21) defines proteins having both "prosequences" and "presequences." However, again, these definitions do not discuss any structural (i.e. sequence) information of the claimed forms of VEGF.

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Similarly, as argued by Appellants on page 13 of the Appeal Brief, the fact that the specification teaches how to obtain the desired protein forms does not demonstrate that Appellants were actually in possession of the protein. The specification simply provides general isolation techniques, which can be used to obtain any desired protein and would not distinguish "mature" or "proprotein" forms from other forms. The fact that certain peer-reviewed journals (Exhibits F and G discussed on page 17 of the Appeal Brief) discuss "mature" and "proprotein" forms of VEGF is, respectfully, not persuasive since patent applications are held to different standards than peer-reviewed journals. The fact that, as argued on page 18 of the Appeal Brief, Exhibit G teaches that the VEGF family undergoes proteolytic processing still does not provide the artisan with the exact amino acid sequence of the mature or proprotein sequence of SEQ ID NO:2.

Finally, Appellants have argued that they have demonstrated that both the 350 amino acid form and the 419 amino acid form of VEGF-2 are identically processed to the mature form of VEGF-2, resulting in the secretion of polypeptides of identical molecular weights, as assessed by SDS PAGE. This argument is also not persuasive since an SDS PAGE gel would only demonstrate that Appellants were in possession of a protein of a particular molecular weight range. The migration of a protein in a gel does not provide the artisan with any information with regard to protein sequence. Basically any protein with a specific molecular weight will migrate to a particular point on a gel. These gels would only demonstrate that the Appellant was in possession of proteins of a particular size. Again, given these gels, the artisan would have at best minimal information regarding the protein sequence (i.e. an estimation of the total number of residues in the protein). Other factors such as post-translational modifications would also affect protein size and, therefore, migration and the artisan would not be able to differentiate, for example, the 'mature' form of SEQ ID NO:2 from a fragment of SEQ ID NO:2, or another protein, with post-translational modifications since these could potentially migrate to the same point on a gel. If gels could be used to show possession, one of skill in the art would simply have to run every human chromosome on

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gels to claim that they were in possession of the entire human genome. It is believed that all pertinent arguments have been addressed.

For the above reasons, it is believed that the rejections should be sustained.

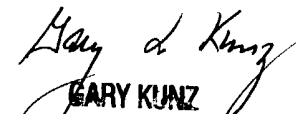

ROBERT LANDSMAN
PATENT EXAMINER

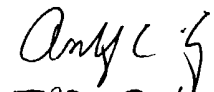
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July 7, 2004

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